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Evaluation of the interval between pregnancies for perinatal outcomes: A Prospective study

Mochhoury Latifa[1], Milouda Chebab[1], Fatima Zahra Laamırı[1], Aicha Yacoutı[1], Amina Barka[1, 2]
[1] Department of Health Sciences and Technologies, Hassan First University of Settat, Settat
[2] Department of Neonatology, Faculty of Medicine and Pharmacy, Mohammed V. University, Rabat, Morocco

Abstract

Aim: The aim of this study is to provide Moroccan data on major outcomes and risk factors of the short interpregnancy intervals.

Material and Methods: We conducted a retrospective study, between June 1, 2020 and June 1, 2021. Thus, we enrolled in our study 1200 patients. The participants were divided into two groups: the first group included women with short intervals between pregnancies (less than 9 months (n=443)), and the second group was the control group, which included women with interpregnancy intervals of more than 9 months (n=187)

Results: A short interval between pregnancies was associated with a high score of prematurity, anemia and low birth (p< 0, 05). Risk factors of the short interpregnancy intervals were age > 35 years, no anterior contraception or breastfeeding, and often low-income background

Discussion: Both preventive strategies during and after pregnancy and appropriate family planning management care are needed to avoid perinatal complications.

Keywords

Short Interpregnancy Intervals, Risk Factors, Prematurity, Anemia, Low Birth

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Corresponding Author: Latifa Mochhoury, Hassan First University of Settat, Higher Institute of Health Sciences, Laboratory of Health Sciences and Technologies, 26000, Settat, Morocco.
E-mail: latifa.mochhoury@uhp.ac.ma P: +21 262 030 35 82
Corresponding Author ORCID ID: https://orcid.org/0000-0002-5019-2296
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Introduction

Research has unveiled that labor complications, such as premature labor, neonatal death and intrauterine growth restriction [1], were associated with childbirths occurring at closer intervals [2-3]. Irregular bleeding, anemia and postpartum infections become more common during the third trimester, which can be explained by maternal iron and folate deficiency [4-5]. Nevertheless, studies have not shown whether this association is due to obstetrical history or demographic factors.

Women whose pregnancies are closely spaced are often disadvantaged, younger, and less educated [1, 2]. Usually, close pregnancies are often associated with youth of patients or with unfavorable socio-economic factors [1]. The latter represent only a part of the risk factors for closely spaced pregnancies, thus making them unsatisfactory and insufficient for the implementation of effective and fruitful prevention.

No studies have been conducted in Morocco on closely spaced pregnancies. Our study aims at exploring maternal risk factors of closely spaced pregnancies, analyzing their possible relationship with maternal-fetal complications, and informing the public of valuable prevention methods.

Material and Methods

This retrospective study was carried out using a descriptive and comparative case-control analysis and was conducted at the Hassan I Provincial Hospital in Settat. This study was carried out according to the ethical rules for medical publication. Medical confidentiality and patient anonymity were respected.

All patients with close pregnancies, with an alive newborn, between June 1, 2020 and June 1, 2021, were identified using birth registers and medical records from the maternity hospital of the provincial hospital center of the city of Settat. Six hundred and thirty patients were selected according to exclusion criteria, such as terminated pregnancies (miscarriage, intrauterine death or termination of pregnancy), twin pregnancies and multiple pregnancy (more than three pregnancies).

Close pregnancies were set to be 9 months between delivery and the conception of a new pregnancy. The date of the start of pregnancy was determined by ultrasound of the first trimester or date of the last menstrual period.

A group of patients (N= 443), which gave birth twice with a time interval between the first delivery and conception of the following pregnancy of less than 9 months was then matched with a control group (N= 187), whose patients had closely spaced pregnancies greater than or equal to 9 months in the same study period and respecting the same exclusion criteria.

Operational Definitions

In our survey, we considered all women living in the town as urban and those living 10 km or further from the city Centre as rural.

Socio-economic level

According to a study conducted in 2007 by the High Commission for Planning (HPC), a net monthly income of less than 3,000 Moroccan Dirhams (MAD) was classified as low, whereas a monthly net income of 3,000 MAD or higher this was classified as high income.

Gestational age was calculated in weeks of amenorrhea (WA) from the date of the last menstruation.

A postpartum hemorrhage was defined as blood loss greater than 500ml in the first 24 hours after delivery.

Pre-eclampsia was defined by the persistence of a systolic blood pressure greater than 140 mm of Hg and/or a diastolic blood pressure greater than 90 mm of Hg and proteinuria greater than 0.3g/24h. Anemia during pregnancy was defined as a hemoglobin level of less than 10g/dl.

Degree of severity of anemia

Anemia was considered mild if (10 Hemoglobin levels <11 dg / l). That was moderate if (7< hemoglobin <10 dg / l) and severe if (hemoglobin ≤ 7 dg / l).

From the medical records, the following neonatal data were collected:

• The child's weight;

• The term of birth in weeks of amenorrhea (WK). Apgar score at five minutes of life, the weight of the newborn, namely hypotrophy (< 10th percentile) or macrosomia (> 90th percentile) (curves of references AUDIPOG [6])

• Neonatal hypothermia persisted at skin temperature below 35 °C.

The following data about the mothers were collected: age, family situation, socio- professional situation, educational level, parity, breastfeeding, as well as the contraceptive method prescribed postpartum after childbirth. For each pregnancy studied, the following were observed: the existence of an obstetric pathology (threat of premature delivery, premature rupture of the membranes, the appearance of amniotic fluid), the mode of childbirth (spontaneous low way or high "cesarean section").

Ethical considerations

Participants were informed that the survey was anonymous and that collection data collection was strictly for scientific purposes. The verbal consent of the participants was requested. Each participant was given the opportunity to discontinue participation if she did not agree. Participants were also reassured that not participating would not affect the progress of their medical care in the hospital.

Data Measurement

Data analysis in this study was performed using Statistical Package for Social Sciences (SPSS) 13.0 (SPSS, Inc., Chicago, IL, USA). Quantitative and qualitative variables were created from the data, which were codified for statistical analysis. Descriptive analysis of the variables was based primarily on class size and proportions, and mean and standard deviations were used as measures of central tendency and dispersion. Regarding the conditions, qualitative variables were compared using the chi-square test or Fisher's exact test. Pearson's correlation test was performed to understand the relationship between quantitative variables. Mean comparison of quantitative variables for different classes of a qualitative variable were performed using the Student's (-test for independent samples, after verification of the different condition of the test. For all statistical tests, a P threshold of <0.05 was considered significant.

Ethical Approval

Ethics Committee approval for the study was obtained.

Results

A total of 1200 patients were admitted; 630 patients were included, classified into 2 categories according to the inclusion and exclusion criteria: group 1, whose interval between pregnancy was less than 9 months (N= 443), and the control group, whose interpregnancy interval was higher than 9 months (N= 187).

Characteristics of the study population are presented in Table 1. The median maternal age was 32 years (± 6.59) for the group of patients whose interpregnancy interval was < 9 months vs 29 years (± 8.40). The difference was significant (p<0.05). In the group of patients with a close pregnancy < 9 months, 53.7% were single vs 43% were in the control group (p <0.05) and 34% had no profession vs 6% in the control group (p < 0.05). In addition, 12.6% were followed versus 6% in the control group, the difference was. In the group of closely spaced pregnancies.

Table 1. Characteristics of the study population

Variable		Interpregnancy interval (MO)		p
		<9 (MO) N= 443 ( ) %	>9 (MO) N=187 ( ) %	
Age (y±sd)		32 (±6.59)	29 (±8.40)	
Maternal age at delivery (year)	<21	(46) 10,4	(73) 39	<0,05*
	21-35	(127) 28,7	(33) 17,6	
	>35	(27) 60,9	(81) 43,3	
Marital status	Married	(205) 46,3	(112) 59,9	<0,05*
	Not married	(238) 53,7	(75) 40,1	
Job	yes	(292) 65,9	(156) 83,4	<0,05*
	no	(151) 34,1	(31) 6,6	
Prenatal care visits	>3	(386) 87,1	(175) 93,6	NS
	<3	(57) 12,9	(12) 6,4	
Residence	rural	(226) 51	(72) 38,5	<0,05*
	urban	(217) 49	(115) 61,5	
Socioeconomic Rank	Low level	(240) 54,2	(37) 19,8	< 0,05*
	High level	(203) 45,8	(150) 80,2	
Education	Primary level	(212) 47,9	(65) 34,8	NS
	Secondary level	(197) 44,5	(107) 57	
	High level	(34) 7,70	(15) 8	
Preterm or Term (wk)	<36	(236) 53,3	(50) 26,7	< 0,05*
	36-40	(72) 16,3	(114) 61	
	>40	(13) 30,4	(23) 12,3	
Previous breastfeeding	no	(41) 293	(108) 57	< 0,05*
	yes	(31) 7	(79) 42	
Iron complement	no	(382) 86,2	(166) 88,8	NS
	yes	(61) 13,8	(21) 11,2	

* Significant (P < 0.05); NS: not significant; Quantitative variables were expressed as mean ± standard deviation, and qualitative variables were expressed as numbers and percentages

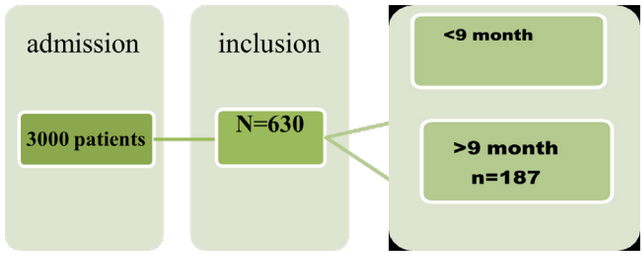

Figure 1. Flow chart of population

The average term of delivery was (36 [±10.3] WA), for the group whose interpregnancy interval < 9 months vs (38[± 3.52 WA]), thus the term < 36 GW was 53, 3% in the population with interbirth interval < 9 months vs 26.7% in the control group (p < 0.001).

For patients who failed contraception, 89% were patients with a close pregnancy < 9 months vs 55.6% in the control group (p < 0.001). Also, 93% did not breastfeed in the group with interpregnancy interval < 9 months vs 57% in the control group ((p <0.05).

Maternal and neonatal complications according to interpregnancy interval are presented in Table 2. The use of the high route was statistically in the group with a close pregnancy of 79% vs 65.8% in the control group. Meconial liquid was 52.6% vs 11.2% (p < 0.05). Also, the premature

Table 2. Maternal and neonatal complications according to interpregnancy interval

variable		interpregnancy interval (mo)		p
		<9 MO N=443 ( ) %	>9 MO N=187 ( ) %	
Birth weight (g±sd)		2999 [±1130]	3079 [±786]	<0,05*
hypothrophia		(224) 50,6	(45) 24,1	
normal		(72) 16,3	(108) 57,8	<0,05*
macrosomia		(147) 33,2	(34) 18,2	
Apgar Score 5min				
>7		(339) 76,50	(187) 100	<0,05*
<7		(104) 23,50	0	
Gender				
Male		(244) 55,1	(106) 56,7	Ns
Female		(199) 44,9	(81) 43,3	
Stillbirth	yes	(19) 4,3	(5) 2,7	Ns
Preterm birth	yes	(237) 53,5	(49) 26,2	<0,05*
Hypothermia	yes	(96) 21,7	(23) 12,3	Ns
Maternal Complications				
Hemorrhage	yes	(32) 7,2	(80) 42, 8	<0,05*
Anemia	yes	(181) 40,9	(11) 5	<0,05*
Preeclampsia	yes	(156) 35	(46) 24	0,01*
Delivery mode	Low way	(93) 21	(64) 34,2	<0,05*
	Cesarean	(350) 79	(123) 65,8	
General anesthesia	Yes	(304) 62,6	(59) 41	<0,05*
AFA	Meconial	(233) 52,6	(21) 11,2	<0,05*
PROM	Yes	(69) 15,6	(18) 9,60	NS

*significant, NS: not significant; Quantitative variables were expressed as mean± standard deviation, and qualitative variables were expressed as numbers and percentages. PROM: Premature rupture of membranes; AFA: amniotic fluid appearance

Table 3. Results of logistic-regression analyses of the interpregnancy interval as a risk factor for low socioeconomic status, age 35, no previous contraception, no breastfeeding

Interpregnancy interval		B	OR	IC à 95 %	P
<9 mo	Const	-5,622			0.00
	age >35 years	2,949	19,079	[4,98; 73,06]	<0,05
	Rural area	-0,76	0,468	[0,28; 0,78]	0,004
	Low socioeconomic status	1,243	3,465	[2,06; 5,81]	<0,05
	no previous contraception	2,758	15,77	[7,31; 33,99]	<0,05
	no breastfeeding	3,901	49,462	[15,78; 155,03]	<0,05

OR: Odds ratio, a p-value < 0.05 is considered significant

rupture of the membranes was predominant in the group whose interpregnancy interval was < 9 months with a percentage of 55.6% vs 9.6% (p < 0.05).

The mean birth weight was 2999 [±1130 g] in patients with a closely spaced pregnancy <9 months, versus 3079 [±786 g] (Table 3). Prematurity in close pregnancies < 9 months was 53.3% vs 26.2% in the control group (p < 0.001) There was a significant difference regarding hypotrophy which was 50.60% vs 24 .1% Similarly, the incidence of hypothermia in the immediate neonatal period in newborns from close pregnancies < 9 months was 21.7% vs 12.3% in the control group. (p=0.007). The percentage of women with pre-eclampsia was 35% in the case group vs. 24% in the control group (p < 0.05). Anemia during pregnancy was 40.9% in patients with a close pregnancy against 5% in the control group (p < 0.05). The incidence of postpartum hemorrhage was 92.8% vs 57.2% in the control group (p < 0.05) (Table 2).

Table 3 shows, according to multivariate logistic regression, that age > 35 years was a risk factor with OR = 19.07; IC 95 [4.98-75.06]; p<0.05. The level low socioeconomic status and coming from a rural area were also risk factors, with a respective OR of 3.46; 95% CI [2.06- 5.81]; p<0.05 and OR = 0.46; 95% CI [0.28-0.78], p<0.05. The fact of not resorting to natural breastfeeding and not adopting contraception during the previous pregnancy were risk factors with a respective OR of 49.46; CI 95 [15.78-155.03]; p<0.05 and OR = 15.77; CI 95 [7.31-33.99]; p <0.05

Discussion

As mentioned above, our study was carried out on close pregnancies, which has proved to be valuable given the lack of data on the topic.

The choice of inclusion of close pregnancies was defined in our study by a delay of less than nine months between the date of the first delivery and the following conception. This delay to define a close pregnancy varies according to the authors between six and 12 months [1-7]. We, therefore, chose an average period of nine months as the selection criterion.

It was observed that the patients in the group whose interval between pregnancies was higher than 9 months, were older, the average age was 32 years ± 6.59. Nearly 60.9% of patients were over 35 years old, against 43.3% of patients in the control group. This observation contradicts the findings, which stated that young age was a risk factor multiplied by 20.3 (95% CI: 4.5-91) for patients aged under 21 [8, 9]. On the other hand, our study confirmed advanced that age (after 30 years) was a risk factor for closely spaced pregnancies in Denmark, and that late pregnancies, in turn, were due to a preponderance of professional activity over family life [10,11]. Indeed, women with a pregnancy after 30 years choose, according to these authors, to shorten the time interval between subsequent pregnancies in order to be able to catch up with menopause. The significantly large proportion of non-breastfeeding women in the closely spaced pregnancy group partly explains the occurrence of closely spaced pregnancies; the "contraceptive barrier" of breastfeeding did not protect the patients. The fact of single people living in a disadvantaged environment and the conditions cited above could impede the follow-up of the pregnancy. Added to this are remote establishments of care, nutrition and contraception.

In our study, hypotrophy and prematurity were found to pose a significant neonatal risk. This can be explained by the partition of cervical insufficiency, which implies a weakness of the tissue when two pregnancies are close together, hence the interest in spacing the interval between genesis, to find the muscle tone of the cervix before you can start a new pregnancy. Our results are in line with both a systematic review and a meta- analysis by Conde-Agudelo et al [12] who reported that interpregnancy intervals of less than 18 months and greater than 60 months are significantly associated with low gestational age birth, despite adjustment for the least maternal age and one marker of socio-economic status. Previous studies have demonstrated that short interpregnancy interval is associated with small gestational age at birth [13]. On the other hand, a cohort study with detailed information on pregnancy intention and socio-economic status, short interpregnancy interval was not associated with lower birth weight. These findings suggest that previously observed associations between short interpregnancy intervals and lower birth weight may reflect the influence of socio-economic and/or other unmeasured factors [14]. The rationale of this could be that mothers with short inter-pregnancy intervals might not recover from physiological changes that happen during pregnancy and after delivery, which is associated with a decrease in macro and micro-nutrients, abnormal remodeling of endometrial blood vessels, anemia, and an increase in the risks of certain other factors inducing adverse perinatal outcomes

Our study is consistent with international studies which have shown that during close pregnancies, women were more anemic, this is particularly the case of the French study, which had highlighted an increased risk of 4.9 for anemia during pregnancy (P=0.001), and an increased risk of 2.1 postpartum (P=0.02) in the closely spaced pregnancies group (interval <9 months) [8].

These factors are linked to nutritional deficiency, in particular iron and folic acid deficiencies [15, 16], the maternal nutritional potential, which would not have had time to regenerate completely. For this reason, during pregnancy monitoring, women should be considered at greater risk of anemia, iron and folic acid supplementation should be offered quickly if necessary. Furthermore, certain prostaglandins, initiators of childbirth, have been incriminated. Smith et al. suggested abnormally high levels of these substances after first delivery and consider them as possible risk factors for premature delivery [17].

Our results confirm those of the literature, in fact, recourse to cesarean section was the majority in the group whose interval <9 months [18]; it is always clear that cesarean delivery is very demanding compared to vaginal delivery, given the urgency imposed by neonatal suffering, or the fact that the pregnancy is desired.

We concluded significant differences in the occurrence of postpartum hemorrhage, which joins Conde's study [12]. The latter confirmed a 70% increased risk when the interval between two pregnancies was less than or equal to 5 months compared to an interval of between 18 and 23 months. The presence of metrorrhagia could be explained by the increased

number of placental abnormalities during close pregnancies [19-22] and a defect in the remodeling of endometrial vessels. Most of our results could be explained by the maternal exhaustion hypothesis, which suggests that short intervals do not allow the mother to recover from the physiological stresses imposed by the previous pregnancy, resulting in depletion of maternal nutrient stores and anemia, which play a role in the pathogenesis of premature rupture of membranes and puerperal endometritis [23-25].

Regarding the increased risk of bleeding in the third trimester, we postulate that a short interval between pregnancies may interfere with the normal processes of endometrial blood vessel remodeling after delivery, with subsequent uteroplacental underperfusion, thereby increasing the likelihood of placental abruption and placenta previa.

Other alternative explanations for the relationship between short intervals between pregnancies and adverse maternal outcomes could be levels of postpartum stress, socioeconomic factors other than marital status and education, unstable lifestyles, occupation, inability to use or inadequate use of health services, and other behavioral or psychological determinants.

Conclusion

Although there is no clear and explicit literary definition of the term 'close pregnancy', it is essential to recognise the complications it can cause. In this regard, our study shed light on the determinants of closely spaced pregnancies and the factors that increase their occurrence (lack of contraception, artificial breastfeeding after the first pregnancy, age >35 years, geographical background and socioeconomic level). However, a large-scale multivariate study is much needed to tackle recommendations of intervals between two pregnancies. Our findings suggest several ways to improve perinatal outcomes. Providers of reproductive health care could counsel mothers on the association between adverse perinatal outcomes and short and long interpregnancy intervals, and on the benefits of optimizing that interval. Public health programs could identify women who become pregnant after short or long interpregnancy intervals. Public health agencies could consider measures to improve family-planning and fertility services.

Limitations of the study

• Incomplete medical records.

• The prevalence of reproductive risk factors was relatively low in our study population, and hence caution should be used in generalizing our results to other populations.

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Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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